(FILE 'HOME' ENTERED AT 07:37:00 ON 11 APR 2003)

FILE 'REGISTRY' ENTERED AT 07:37:06 ON 11 APR 2003
L1 STRUCTURE UPLOADED
L2 0 S L1
L3 157 S L1 FUL

FILE 'CAPLUS, USPATFULL' ENTERED AT 07:38:28 ON 11 APR 2003
L4 58 S L3
L5 59727 S (MAG OR MYELIN ASSOC? GLYCOPROTEIN)(3A)(PROMOT? OR EXPRESS?)
L6 1 S L4 AND L5

=> dup rem l4
PROCESSING COMPLETED FOR L4
L7 58 DUP REM L4 (0 DUPLICATES REMOVED)

=> d l4 1-58 bib,abs

L4 ANSWER 1 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 2001:868218 CAPLUS
DN 136:694
TI Thromboxane inhibitors, compositions, and methods for therapeutic use
IN Saenz de Tejada, Inigo
PA Nitromed, Inc., USA
SO PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001089519	A1	20011129	WO 2001-US16318	20010522
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2003050305	A1	20030313	US 2002-285620	20021101
PRAI	US 2000-205536P	P	20000522		
	WO 2001-US16318	A1	20010522		

OS MARPAT 136:694
AB The invention describes methods for treating or preventing sexual dysfunctions in males and females, and for enhancing sexual responses in males and females, by administering a therapeutically effective amt. of at least one thromboxane inhibitor, and, optionally, at least one compd. that donates, transfers, or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase, and/or at least one vasoactive agent. The male or female may preferably be diabetic. The invention also provides compns. comprising at least one thromboxane inhibitor, and, at least one compd. that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase, and, optionally, at least one therapeutic agent, such as, vasoactive agents, nonsteroidal antiinflammatory compd.

(NSAIDs), selective cyclooxygenase-2 (COX-2) inhibitors, anticoagulants, angiotensin converting enzymes (ACE) inhibitors, angiotensin II receptor antagonists, renin inhibitors, and mixts. thereof. The invention further provides methods for treating or preventing ischemic heart disorders, myocardial infarction, angina pectoris, stroke, migraine, cerebral hemorrhage, cardiac fatalities, transient ischemic attacks, complications following organ transplants, coronary artery bypasses, angioplasty, endarterectomy, atherosclerosis, pulmonary embolism, bronchial asthma, bronchitis, pneumonia, circulatory shock of various organs, nephritis, graft rejection, cancerous metastases, pregnancy-induced hypertension, preeclampsia, eclampsia, thrombotic and thromboembolic disorders, intrauterine growth, gastrointestinal disorders, renal diseases and disorders, disorders resulting from elevated uric acid levels, and dysmenorrhea, and for inhibiting platelet aggregation or platelet adhesion or relaxing smooth muscles. The compds. and/or compns. of the present invention can also be provided in the form of a pharmaceutical kit.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 2000:907033 CAPLUS
DN 134:51387
TI Synergistic anti-inflammatory, antiallergy, and antiasthmatic agents for treatment of arachidonate metabolism disorders
IN Kawahara, Yoshikazu; Ohmori, Hiromasa
PA Nikken Chemicals Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2000355551	A2	20001226	JP 1999-168017	19990615
PRAI JP 1999-168017		19990615		

AB The agents contain leukotriene-synthesizing enzyme inhibitors and thromboxane-synthesizing enzyme inhibitors. Concomitant administration of ZD-2138 and isbogrel to guinea pigs sensitized with egg white albumin resulted in 49.5% inhibition of airway contraction, vs. 6.8% and 18.3%, for ZD-2138 and isbogrel alone, resp.

L4 ANSWER 3 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 2000:841978 CAPLUS
DN 134:13340
TI Myelin-associated glycoprotein (MAG) expression promoters
IN Kawasaki, Masakazu; Gotoh, Nobuharu; Hayashi, Yoshiharu; Kawasaki, Kazuyuki
PA Welfide Corporation, Japan
SO PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

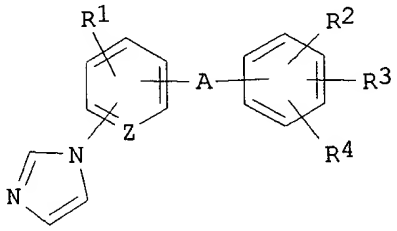
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000071119	A1	20001130	WO 2000-JP3373	20000525

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE,

SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1186296	A1	20020313	EP 2000-931568	20000525	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
BR 2000011551	A	20020402	BR 2000-11551	20000525	
NO 2001005733	A	20020111	NO 2001-5733	20011123	
PRAI JP 1999-144336	A	19990525			
WO 2000-JP3373	W	20000525			

OS MARPAT 134:13340
GI



I

AB Disclosed is myelin-assocd. glycoprotein (MAG) expression promoters contg. compds. I [R1 = H, halogen, alkyl, alkoxy; R2, R3 = H, alkyl; R4 = alkyl, COOH, COOR5, CONR6R7, CH2NR6R7, CH2OH, CH2OR8 (R5, R8 = alkyl; R6, R7 = H, alkyl, imidazole); A = CH(OH); CO, CH2; Z = CH, N], optically active isomers thereof or their pharmaceutically acceptable salts. As an example of the compds. represented by the general formula I, 4-[.alpha.-hydroxy-5-(1-imidazoyl)-2-methylbenzyl]-3,5-dimethylbenzoic acid may be cited. These MAG expression promoters are useful as preventives and/or remedies for diseases of mammals including humans mainly presenting myelin hypoplasia and, in its turn, myelin sheath hypoplasia or myelin sheath destruction. A compd. Y-128 promoted axon myelination and MAG expression in Schwann cell/dorsal root ganglia (DRG) cell cocultures.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1998:527320 CAPLUS
DN 129:148981
TI Process for producing optically active imidazole derivatives and intermediates therefor
IN Kawasaki, Kazuyuki; Kobayashi, Haruhito; Ehara, Syuji; Sato, Hideaki
PA Yoshitomi Pharmaceutical Industries, Ltd., Japan
SO PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

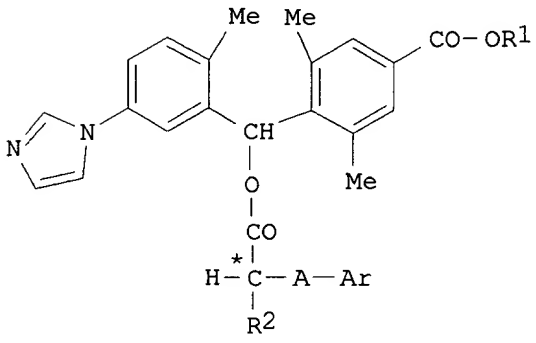
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9832740	A1	19980730	WO 1998-JP150	19980114

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,

DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

JP 2000290259	A2	20001017	JP 1997-10114	19970123
AU 9854966	A1	19980818	AU 1998-54966	19980114
EP 972768	A1	20000119	EP 1998-900397	19980114
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6066739	A	20000523	US 1999-355096	19990723
US 6166221	A	20001226	US 2000-511782	20000223
PRAI JP 1997-10114	A	19970123		
WO 1998-JP150	W	19980114		

OS CASREACT 129:148981; MARPAT 129:148981
GI



I

AB A process for producing optically active 4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoic acid or pharmacol. acceptable salts thereof comprises optically resolving compds. represented by general formula I [R1 = alkyl, etc.; R2 = alkyl, phenylalkyl; Ar = (un)substituted Ph, etc.; A = bond, NHSO2; * indicates the (S) or (R) configuration] by fractional crystn. to give the optically active isomer thereof and then hydrolyzing the isomer. This process can provide a resoln. method useful for industrially mass-producing the optically active isomer of 4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoic acid which is useful as a thromboxane synthesis inhibitor and a preventive/remedy for diabetic complications.

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1997:543473 CAPLUS
DN 127:140555
TI Preventives and remedies for complications of diabetes
IN Hayashi, Yoshiharu; Goto, Nobuharu
PA Yoshitomi Pharmaceutical Industries, Ltd., Japan; Hayashi, Yoshiharu; Goto, Nobuharu
SO PCT Int. Appl., 29 pp.
CODEN: PIXXD2

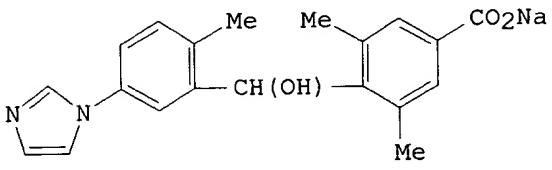
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9724333	A1	19970710	WO 1996-JP3776	19961224
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2241856	AA	19970710	CA 1996-2241856	19961224
AU 9711735	A1	19970728	AU 1997-11735	19961224
AU 716332	B2	20000224		
EP 881218	A1	19981202	EP 1996-942640	19961224
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1209122	A	19990224	CN 1996-180052	19961224
CN 1092645	B	20021016		
BR 9612316	A	19990713	BR 1996-12316	19961224
NZ 324454	A	20000929	NZ 1996-324454	19961224
RU 2173148	C2	20010910	RU 1998-113956	19961224
EE 3524	B1	20011015	EE 1998-208	19961224
NO 9802988	A	19980826	NO 1998-2988	19980626
US 6060496	A	20000509	US 1998-91993	19980626
US 6258834	B1	20010710	US 2000-498481	20000204
CN 1324618	A	20011205	CN 2001-117254	20010426
US 2001036957	A1	20011101	US 2001-850000	20010508
US 2002169194	A1	20021114	US 2002-80660	20020225
PRAI JP 1995-340161	A	19951227		
WO 1996-JP3776	W	19961224		
US 1998-91993	A3	19980626		
US 2000-498481	A3	20000204		
US 2001-850000	B1	20010508		

AB This document discloses (a) preventives and remedies for complications of diabetes contg. as the active ingredient 4-[.alpha.-hydroxy-2-methyl-5-(1-imidazolyl)benzyl]-3,5-dimethylbenzoic acid, optical isomers thereof or pharmaceutically acceptable salts thereof; (b) and a method for preventing or treating complications of diabetes by administering the above compds. in an efficacious dose. These drugs are useful in the prevention and treatment of complications of diabetes such as diabetic neuropathy, nephropathy, ocular disorders and arterial sclerosis. Moreover, they can exhibit long lasting effects even in an extremely small dose, which makes it possible to take the drugs only once a day. The bioactivity of 4-[.alpha.-hydroxy-2-methyl-5-(1-imidazolyl)benzyl]-3,5-dimethylbenzoic acid in a variety of diabetes models is given in this document: this compd. showed potent therapeutic effect at 1 mg/kg in rats. Formulations contg. compds. of this invention are given.

L4 ANSWER 6 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1994:314966 CAPLUS
DN 120:314966
TI Y-20811: a long-acting thromboxane A2 synthase inhibitor
AU Matsumoto, Yasuhiro; Mikashima, Hiroshi
CS Tokyo Res. Lab., Yoshitomi Pharm. Ind., Saitama, Japan
SO Cardiovascular Drug Reviews (1993), 11(3), 283-98
CODEN: CDREEA; ISSN: 0897-5957

DT Journal; General Review
LA English
GI

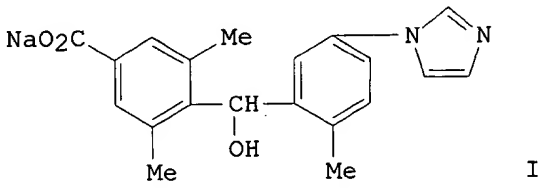


I

AB A review with 53 refs. Chem. and pharmacol. of the long-acting thromboxane A2 synthase inhibitor, Y-20811 (I), are discussed.

L4 ANSWER 7 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1994:182679 CAPLUS
DN 120:182679
TI Effect of Y-20811, a thromboxane A2 synthetase inhibitor, on the arachidonic acid-induced response in the blood-superfused canine coronary artery
AU Matsumoto, Yasuhiro; Noguchi, Yutaka; Inui, Jun
CS Tokyo Res. Lab., Yoshitomi Pharm. Ind., Ltd., Iruma, 358, Japan
SO Nippon Yakurigaku Zasshi (1994), 103(2), 59-66
CODEN: NYKZAU; ISSN: 0015-5691
DT Journal
LA Japanese
AB Effects of Y-20811, a thromboxane A2 synthetase inhibitor, on the arachidonic acid (AA)-induced responses were investigated in the isolated canine coronary artery superfused with blood from a donor dog and Krebs-Henseleit soln. When the coronary artery was superfused with Krebs-Henseleit soln., AA did not have any remarkable effect on its tone. In the coronary artery superfused with blood, AA (10-100 .mu.g) caused phasic constriction followed by relaxation. After denudation of the endothelium, the contractile response was augmented, and the relaxant effect was abolished. Y-20811 (1 mg/kg, i.v.), administered to the donor dog, inhibited the contraction and augmented the relaxation. Indomethacin (5 mg/kg, i.v.) and aspirin (30 mg/kg, i.v.) also inhibited the AA-induced contraction. Indomethacin inhibited the relaxation induced by AA (10-100 .mu.g), whereas aspirin inhibited the relaxation induced by a low dose of AA (10-30 .mu.g). These results suggest that Y-20811 inhibits the TXA2-induced contraction and augments the prodn. of the relaxant metabolite of AA in the coronary artery.

L4 ANSWER 8 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1993:485685 CAPLUS
DN 119:85685
TI Effect of Y-20811, a thromboxane synthetase inhibitor, on photochemically induced cerebral embolism in rabbits
AU Fujimura, M.; Mikashima, H.
CS Res. Lab., Yoshitomi Pharm. Ind. Ltd., Yoshitomi, 871, Japan
SO Thrombosis Research (1993), 70(3), 233-44
CODEN: THBRAA; ISSN: 0049-3848
DT Journal
LA English
GI



I

AB The effect of Y-20811 (I), a selective thromboxane A2 synthetase inhibitor, was investigated on cerebral embolism using a new model of embolic cerebral infarction in rabbits. Most of cerebral infarctions were obsd. in the hemisphere, ipsilateral to the irradiated carotid artery. Cerebral infarction, ranging from 0.2 to 1.0 mm in size, appeared only on the surface of the cortex. The platelet emboli were identified in the carotid artery and cortex arteriole by light microscopy. In this study, 83% of the control group had cerebral infarction. Y-20811 significantly suppressed the infarction no. and the incidence at doses of 1 mg/kg and 10 mg/kg (p.o.), resp. Aspirin significantly inhibited the infarction no. at a dose of 10 mg/kg, but its inhibitory effect decreased at 30 mg/kg. Ticlopidine showed no effect even at a dose of 300 mg/kg. These results indicate that Y-20811 may be useful in preventing embolic cerebral infarction and transient ischemic attacks.

L4 ANSWER 9 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1993:225217 CAPLUS
DN 118:225217
TI Effect of the combination of anticoagulant and thromboxane synthetase inhibitor (Y-20811) or receptor blockade (S-1452) on preventing thrombotic cyclic coronary flow reduction in dogs with coronary stenosis
AU Fujii, Takashi; Matsuzaki, Masunori; Oda, Tsuyoshi; Sakai, Hisanori; Tanaka, Nobuaki; Yano, Masafumi; Miura, Toshiro; Kohno, Michihiro; Katayama, Kazuhiro; Kusukawa, Reizo
CS Sch. Med., Yamaguchi Univ., Ube, Japan
SO Japanese Circulation Journal (1992), 56(11), 1191-7
CODEN: JCIRA2; ISSN: 0047-1828
DT Journal
LA English
AB We examd. the hypothesis that combined actions of anticoagulant (heparin) and Y-20811, thromboxane A2 synthetase inhibitor (TXSI), or S-1452, receptor blockade (TXRB), can provide better antithrombotic protection than TXSI or TXRB alone. In 20 of 33 dogs instrumented, placement of a crit. stenosis at a focus of coronary vascular injury initiated a reproducible cyclic coronary flow redn. (CCFR). TXSI (1 mg/kg, IV) perfectly inhibited CCFR in 6 of 10 dogs (60%0, and was assocd. with a significant decrease in 11-dehydro-TXB2 (85% of control) and an increase in 6-keto-PGF1.alpha. (155%) in coronary sinus blood samples. In the remaining 4 dogs, addnl. administration of heparin (2000 IU) completely abolished CCFR. On the other hand, TXRB (1 mg/kg, IV) perfectly inhibited CCFR in 7 of 10 dogs (70%), and was accompanied by a significant increase in 6-keto-PGF1.alpha. (214%) and unchanged TXB2 level. In the remaining 3 dogs, addnl. administration of heparin (2000 IU) completely abolished CCFR. Thus, the combination of anticoagulant and TXSI or TXRB were more effective than TXSI or TXRB alone in abolishing thrombotic CCFR, suggesting that the combination might be effective for treating patients with impending myocardial infarction.

L4 ANSWER 10 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1993:183119 CAPLUS
DN 118:183119

TI Effects of a thromboxane synthetase inhibitor, Y-20811, on infarct size, neutrophil accumulation, and arrhythmias after coronary artery occlusion and reperfusion in dogs

AU Sato, Naoki; Endo, Takao; Kiuchi, Kaname; Hayakawa, Hirokazu
CS 1st Dep. Intern. Med., Nippon Med. Sch., Tokyo, 113, Japan

SO Journal of Cardiovascular Pharmacology (1993), 21(3), 353-61
CODEN: JCPCDT; ISSN: 0160-2446
DT Journal
LA English

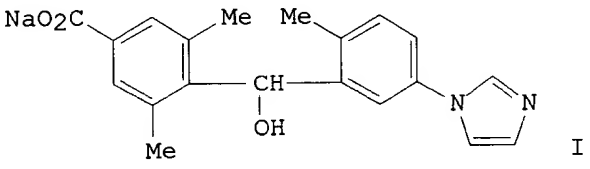
AB To examine effects of a new thromboxane synthetase inhibitor, Y-20811, on infarct size, neutrophil accumulation, and arrhythmias, coronary artery was occluded for 90 min and reperfused for 6 h in anesthetized dogs. Y-20811 administered i.v. 30 min before occlusion decreased serum thromboxane B2 (TBX2) formation by 98% 30 min later and by 79% at 6 h after reperfusion. Ventricular fibrillation (VF) developed in 1 of 15 control and 3 of 10 treated dogs during occlusion (p = NS), whereas after reperfusion it occurred in 7 of 14 control and none of seven treated dogs. The no. of arrhythmias during the first hour of reperfusion was significantly reduced in treated dogs (134 beats/min in control vs. 14 beats/min in treated dogs). Hemodynamics, area at risk, and collateral flow to the ischemic region were similar for the two groups. The extent of myocardial necrosis was 28.0% of the area at risk in control dogs and 27.6% in treated dogs. The relation between the ratio of myocardial necrosis to area at risk and collateral flow was similar. The degree of neutrophil accumulation did not differ but correlated with infarct size. Thus, Y-20811 reduced reperfusion arrhythmias but failed to limit infarct size and neutrophil accumulation after coronary artery occlusion/reperfusion in dogs.

L4 ANSWER 11 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1993:32705 CAPLUS
DN 118:32705
TI Effects of antithrombotic drug, Y-20811 on mural thrombus formation and intimal thickening following intimal injury

AU Hayashi, Tohru; Asada, Yujiro; Kisanuki, Atsushi; Sumiyoshi, Akinobu
CS 1st Dep. Pathol., Miyazaki Med. Coll., Miyazaki, 889-16, Japan

SO Thrombosis Research (1992), 67(1), 81-94
CODEN: THBRAA; ISSN: 0049-3848
DT Journal
LA English

GI



I

AB Inhibitory effect of Y-20811 (I) on platelet thrombus formation induced by mech. intimal injury and subsequent intimal fibrous thickening was studied. In the short term expt., polyethylene tubing was inserted into the rabbit aorta and was drawn out one hour after with or without Y-20811 administration, then the rabbits were sacrificed. In the expt. for the quant. anal. of platelet adhesion, 51Cr-labeled platelets were used. Radioactivities of 2-cm length of the injured segment of the thoracic aorta and the proximal 2cm of the normal segment were measured.

Radioactivity of the injured segment was significantly lower in rabbits treated with Y-20811 than the control ones. The mean thickness (area of thrombi/length of injured intima) and the maximal thickness of the mural thrombi in the Y-20811-treated rabbits were significantly lower than those in control rabbits. De-endothelialized areas showed raised platelet thrombi in the control group and diffuse thin-layered platelet sheets in Y-20811-treated rabbits. In the long-term expt., polyethylene tubing was in-dwelling for 24 h. Rabbits were sacrificed 10 days after drawing out the tubing. Through the expt. Y-20811 was injected i.v. every 24 h. There was no significant difference between the control group and the Y-20811-treated one in both mean thickness and maximal thickness of the intimal fibromuscular thickening. The expts. indicate that Y-20811 has an inhibitory effect on platelet thrombus formation following the intimal injury, but subsequent myointimal thickening is not inhibited by the drug.

L4 ANSWER 12 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1993:20295 CAPLUS
DN 118:20295
TI Photochemically induced thrombosis of the rat coronary artery and functional evaluation of thrombus formation by occurrence of ventricular arrhythmias. Effects of acetylsalicylic acid and a thromboxane A2 synthetase inhibitor of thrombus formation
AU Fukuchi, Miho; Uematsu, Toshihiko; Araki, Seiichi; Nakashima, Mitsuyoshi
CS Sch. Med., Hamamatsu Univ., Hamamatsu, 431-31, Japan
SO Naunyn-Schmiedeberg's Archives of Pharmacology (1992), 346(5), 550-4
CODEN: NSAPCC; ISSN: 0028-1298
DT Journal
LA English
AB During i.v. infusion of rose bengal (48 mg/kg/h), the proximal portion of the rat left coronary artery was illuminated from the outside of the myocardium by green light (540 nm) to produce a transluminal thrombus subsequent to endothelial damage. The primary endothelial damage within the illuminated vascular portion, which resulted from the photochem. reaction between the dye and green light, and the subsequent formation of transluminal blood platelet-rich thrombus, were easily revealed by both light and electron microscopy. The thrombus formation was accompanied by the occurrence of heart ventricular arrhythmias due to myocardial ischemia. The times required to initiate ventricular premature beats (VPBs) and ventricular tachycardia (VT) were 381 and 444 s, resp. Pretreatment of rats with acetylsalicylic acid (3 and 10 mg/kg i.v.) before the initiation of illumination had no effect on the times required to exhibit the first VPBs and VT; the incidences of both types of arrhythmias were not reduced and the thrombus was finally formed. Pretreatment with Y-20811, a TXA2 synthetase inhibitor (0.3, 1, and 3 mg/kg i.v.), delayed the onset of both VPB and VT in a dose-dependent manner. The incidences of VPBs and VT were reduced at 1 and 3 mg/kg, and the thrombus formation was prevented. The formation of a transluminal thrombus in the left coronary artery by the present technique was highly reproducible and could be functionally evaluated by the occurrence of ventricular arrhythmias.

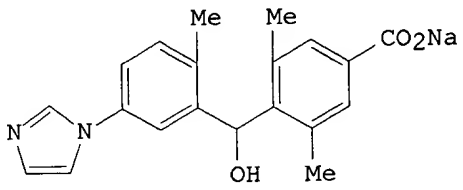
L4 ANSWER 13 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1992:584601 CAPLUS
DN 117:184601
TI Arterial thrombosis model with photochemical reaction in guinea pig and its property
AU Takiguchi, Y.; Hirata, Y.; Wada, K.; Nakashima, M.
CS Sch. Med., Hamamatsu Univ., Hamamatsu, 431-31, Japan
SO Thrombosis Research (1992), 67(4), 435-45
CODEN: THBRAA; ISSN: 0049-3848

DT Journal
LA English
AB The authors have already developed an arterial thrombosis model in the rat femoral artery which utilizes a photochem. reaction between systemically injected rose bengal and transillumination with 540 nm green light from the outside of the vessel. The present study applied this model to guinea-pigs in order to produce a more suitable thrombus model for evaluation of antithrombotic drugs which act on the prostaglandin cascade. In the guinea-pig, the irradiated femoral artery was completely occluded 7 min after the injection of rose bengal (10 mg/kg) in a similar manner as in rats. The processes of primary endothelial injury and the subsequent formation of thrombi during this manipulation were obsd. by the electron microscopy. Pretreatment with aspirin and Y-20811, a thromboxane synthetase inhibitor, significantly prolonged the time required for occlusion in guinea-pigs, while these drugs were ineffective in the rats. The antithrombotic effect of vapiprost, a thromboxane A2 receptor antagonist, was more pronounced in the guinea-pigs than the rats. In conclusion, this model in guinea-pigs is more suitable for evaluating antithrombotic drugs, particularly, the action of which is exerted involving the prostaglandin cascade.

L4 ANSWER 14 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1992:400587 CAPLUS
DN 117:587
TI Effects of Y-20811, a thromboxane A2 synthetase inhibitor, on experimentally induced coronary thrombosis in anesthetized dogs
AU Matsumoto, Yasuhiro; Ochi, Hiroshi; Aihara, Kenichi; Inui, Jun; Ikegami, Kiyoteru
CS Yoshitomi Pharm. Ind., Ltd., Iruma, 358, Japan
SO European Journal of Pharmacology (1992), 213(2), 167-70
CODEN: EJPHAZ; ISSN: 0014-2999
DT Journal
LA English
AB The effects of Y-20811, a selective inhibitor of thromboxane A2 (TXA2) synthetase, on blood flow and local levels of immunoreactive thromboxane B2 (i-TXB2) and 6-keto prostaglandin F1.alpha. (i-6-keto PGF1A) in the coronary artery were investigated in the canine model of coronary thrombosis. Thrombosis was induced by applying an elec. current to the intraluminal surface of the coronary artery. The plasma levels of i-TXB2 and i-6-keto PGF1.alpha. were measured distal to the electrode. In the control group, coronary blood flow decreased and finally stopped 207 min after the start of current application. The level of i-TXB2 rose before the coronary occlusion. Coronary blood flow did not change in the Y-20811-treated group (1 mg/kg i.v.). The level of i-TXB2 decreased and remained lower than that in the control group. The level of i-6-keto PGF1.alpha. tended to increase slightly in the Y-20811-treated, but not in the control group. The wt. of the thrombus in the Y-20811-treated group was less than that in the control group. These results suggest that Y-20811 prevents coronary thrombosis by the inhibition of TXA2 prodn. around the elec. injured lumen of the coronary artery.

L4 ANSWER 15 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1992:166056 CAPLUS
DN 116:166056
TI Effect of Y-20811, a long-lasting thromboxane A2 synthetase inhibitor, on antigen-induced airway hyperresponsiveness in guinea pigs
AU Kagoshima, Masahiko; Tomomatsu, Noriko; Aratani, Hidekazu; Terasawa, Michio
CS Res. Lab., Yoshitomi Pharm. Ind., Fukuoka, 871, Japan
SO International Archives of Allergy and Applied Immunology (1991), 96(3),

238-43
CODEN: IAAAAM; ISSN: 0020-5915
DT Journal
LA English
GI



I

AB The effect of Y-20811 (I) on airway hyperresponsiveness was studied in sensitized guinea pigs. Airway hyperresponsiveness to acetylcholine (ACh) reached max. 7 h after antigen challenge in guinea pigs sensitized actively. I (0.3-3 mg/kg) administered orally 3 h prior to challenge inhibited this airway hyperresponsiveness in a dose-dependent manner. I (3 mg/kg) administered orally 4 h after antigen challenge also decreased the airway hyperresponsiveness. On the other hand, I did not affect the bronchoconstriction induced by ACh, serotonin and histamine in nonsensitized guinea pigs. The no. of eosinophils in bronchoalveolar lavage fluid in the guinea pig reached the peak 7 h after antigen challenge. I had a tendency to decrease the no. of total cells, macrophages and eosinophils in a dose-dependent manner. I suppress the asthmatic mechanism which causes antigen-induced airway hyperresponsiveness.

L4 ANSWER 16 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1992:143580 CAPLUS
DN 116:143580
TI Irreversible inhibition of thromboxane (TX) A2 synthesis by Y-20811, a selective TX synthetase inhibitor
AU Mikashima, Hiroshi; Ochi, Hiroshi; Muramoto, Yoshito; Hirotsu, Kyouichi; Arima, Noriyuki
CS Res. Lab., Yoshitomi Pharm. Ind. Ltd., Fukuoka, 871, Japan
SO Biochemical Pharmacology (1992), 43(2), 295-9
CODEN: BCPCA6; ISSN: 0006-2952
DT Journal
LA English
AB Since Y-20811 has been reported to inhibit serum thromboxane (TX) A2 prodn. with a long duration of action, its mechanism of action was investigated. When [3H]Y-20811 (3 mg/kg) was administered orally to rats, the peak platelet concn. of Y-20811 was obtained 1 h after the administration, and the T1/2 was 43 h. The peak plasma concn. of Y-20811 was also obtained 1 h after administration, but the elimination of Y-20811 from plasma was faster (T1/2.alpha. = 1.5 h, T1/2.beta. = 15 h) than that obsd. in platelets. Serum TXA2 (estd. as TXB2) prodn. was inhibited from 1 to 72 h after the oral administration of unlabeled Y-20811 (3 mg/kg), which temporally resembled the change of the platelet Y-20811 concn. In platelet-rich plasma, [3H]Y-20811 completely inhibited TXA2 prodn. at about 1500 pg/109 platelets, and the IC50 level was about 600 pg/109 platelets, which was similar to values obtained in ex vivo studies. In addn., inhibition of TXA2 prodn. by Y-20811 still remained after washing the drug-pretreated microsomes, whereas that of dazoxiben completely disappeared. A similar irreversible inhibition of TXA2 prodn. was obsd.

with aspirin. These results suggest that Y-20811 may firmly combine with platelet TX synthetase and may irreversibly inhibit TXA2 prodn.

L4 ANSWER 17 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1991:407736 CAPLUS
DN 115:7736
TI Chromatographic separation of optically-active isomers
IN Sakai, Junichi; Ikeda, Kuniki; Hamazaki, Toshio; Kono, Hisashi; Ogawa, Takayuki; Matsumoto, Takashi
PA Yoshitomi Pharmaceutical Industries, Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 03027326	A2	19910205	JP 1989-134256	19890526
	JP 07080793	B4	19950830		
PRAI	JP 1989-134256		19890526		

AB Optically-active isomers are chromatog. sepd. using polysaccharide substituted-arom. carbamate deriv. as a chiral stationary phase and a mixt. of H2O-sol. org. solvents and H2O or buffers contg. various salts as a mobile phase. Na (.+-.)-4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-2,5-dimethylbenzoate dihydrate was charged on a column packed with cellulose tris(3,5-dimethylphenyl)carbamate and eluted with a mixt. of a NaClO4-HClO4 buffer and MeCN, vol. ratio, sepn. factor, and sepn. rate were 4.64, 1.57, and 2.68, resp.

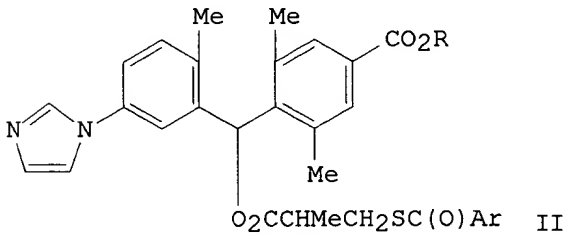
L4 ANSWER 18 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1991:400544 CAPLUS
DN 115:544
TI Effects of Y-20811, a specific thromboxane A2 synthetase inhibitor, on chemical mediator-induced bronchoconstriction in guinea pigs
AU Kagoshima, Masahiko; Tomomatsu, Noriko; Fukuda, Tetsuko; Mikashima, Hiroshi; Terasawa, Michio
CS Yoshitomi Pharm. Ind., Ltd., Fukuoka, 871, Japan
SO Nippon Yakurigaku Zasshi (1991), 97(5), 277-86
CODEN: NYKZAU; ISSN: 0015-5691
DT Journal
LA Japanese
AB The effects of Y-20811 on chem. mediator-induced bronchoconstriction and the release of chem. mediators into lung perfusion fluid during arachidonic acid (AA)-induced bronchoconstriction were examd. in guinea pigs. Y-20811 (0.01-1 mg/kg, i.v.), like acetylsalicylic acid or indomethacin, dose-dependently suppressed arachidonic acid- and LTD4-induced bronchoconstriction, and it (1 mg/kg, i.v.) also inhibited PAF-induced bronchoconstriction in guinea pigs. However, at a dose of 1 mg/kg, i.v., it was inactive against the bronchoconstriction induced by histamine, serotonin, and acetylcholine in guinea pigs. Y-20811 (0.3-10 mg/kg) administered orally also prevented the LTD4-induced bronchoconstriction in a dose-dependent manner. This protective effect of Y-20811 (10 mg/kg, p.o.) persisted for at least 24 h. Y-20811 (10 mg/kg, p.o.) also inhibited antigen-induced bronchoconstriction in guinea pigs passively sensitized with anti-ovalbumin guinea pig serum and pretreated with mepyramine. In the perfused and ventilated guinea pig lungs, Y-20811 inhibited AA-induced bronchoconstriction, decreased the release of TXA2 (estd. as TXB2), and increased the release of PGE2 into the perfused lung fluid, significantly (TXB2 and PGE2 were measured by HPLC). Therefore, Y-20811 suppressed various stimulant-induced bronchoconstrictions through

the decrease of TXA2 prodn. and the increase of PGE2 prodn. Thus, Y-20811 should prove useful as an antiasthmatic drug.

L4 ANSWER 19 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1991:101990 CAPLUS
DN 114:101990
TI Preparation of optically active 4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoic acid by separation of diastereoisomeric esters
IN Tsuruta, Mineo; Oe, Takanori; Shiotsuki, Yoshiko; Matsumoto, Takashi; Yokobe, Tetsuro
PA Yoshitomi Pharmaceutical Industries, Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 02215771	A2	19900828	JP 1989-35684	19890214
PRAI JP 1989-35684		19890214		

OS MARPAT 114:101990
GI



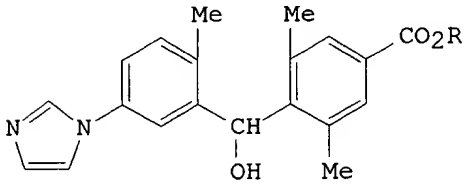
II

AB Racemic title compd. (I), known thromboxane synthase inhibitor useful for treatment of thrombosis, asthma, and nephritis (no data), is resolved by sepn. of its diastereoisomeric esters [II; R = lower alkyl, (substituted) phenylalkyl; Ar = (substituted) Ph, naphthyl, thienyl, furyl, or pyridyl; C* having (S)-(-) or (R)-(+) configuration] on a column chromatog. followed by hydrolysis. Thus, benzylation of (.+-.)-4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoic acid Na salt with 2-ClC6H4CH2Cl in DMF at 45-50.degree. and esterification of the resulting 2-chlorobenzyl ester with (S)-(-)-2-methyl-3-(3,5-dinitrobenzoylthio)propionyl chloride in pyridine/CH2CH2 gave (S)-(-)-I [R = CH2C6H4Cl-2, Ar = C6H3(NO2)2-3,5] which (67 g) was subjected to a silica gel chromatog. eluting with a 200:3:3 mixt. of EtOAc-MeOH-H2O to give 26 g (+)-diastereoisomeric ester and 24.1 g (-)-diastereoisomeric ester which were deacylated with EtONa in EtOH to give (-)-I and (+)-I, resp.

L4 ANSWER 20 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1990:637668 CAPLUS
DN 113:237668
TI Effect of additives on the dissolution of Y-20811, a new thromboxane synthetase inhibitor
AU Shiotsuki, Takako; Kino, Shigemi; Ogawa, Kenji; Yokobe, Tetsuo
CS Res. Lab., Yoshitomi Pharm. Ind., Ltd., Fukuoka, 871, Japan
SO Yakuzaigaku (1990), 50(2), 107-12
CODEN: YAKUA2; ISSN: 0372-7629

09/979,509

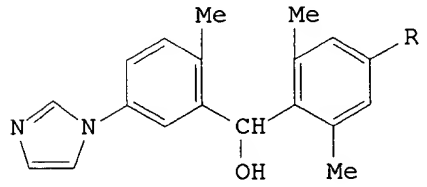
DT Journal
LA English
GI



I, R=Na
II, R=H @ H_2SO_4

AB Compressed tablets of Y-20811 (I) and sulfate salt (II) were prepd. and their dissoln. behaviors from tablets compared. The dissoln. rate of active ingredients from tablets contg. I was significantly higher than those contg. II. A great increase in the dissoln. rate was obsd. when tablets of I were prepd. with NaHCO3, D-mannitol and a water-sol. polymer such as polyvinylpyrrolidone K-30 (PVP K-30) or hydroxypropyl cellulose-L (HPC-L). In order to improve the dissoln. rate of the drug, fine granules of I were prepd. with some additives, by referring the formulation of the above tablets. The addn. of NaHCO3 and HPC-L to the granules facilitated significantly the drug-release in the dissoln. media over the pH range of 1.2 to 6.5. The enhancing effects of NaHCO3 and HPC-L may be ascribable to a increase in microenvironmental pH around granules and an inhibition of the deposition of I after acid dissoln., resp.

L4 ANSWER 21 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1990:637667 CAPLUS
DN 113:237667
TI Dissolution and absorption characteristics of new thromboxane synthetase inhibitors
AU Iwata, Toshio; Akiyama, Yohichi; Shiotsuki, Takako; Iwata, Akihiro; Isobe, Masao; Takamatsu, Rikuo; Yokobe, Tetsuo
CS Res. Lab., Yoshitomi Pharm. Ind., Ltd., Fukuoka, 871, Japan
SO Yakuzaigaku (1990), 50(2), 101-6
CODEN: YAKUA2; ISSN: 0372-7629
DT Journal
LA English
GI

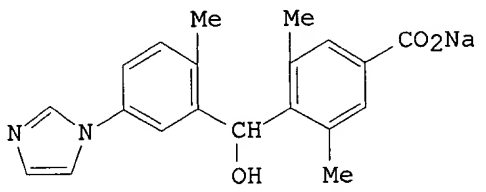


I, R=CO_2H
II, R=Me

AB The in vitro dissoln. characteristics of five new thromboxane synthetase inhibitors were evaluated by using the pH controlled dissoln. system which can mimic the physiol. pH conditions in the gastrointestinal tract. The Na salt and the sulfate of 4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoic acid (I) were dissolved rapidly in the acidic medium and remained stable in soln. even in the neutral medium,

while the dissoln. of I was insufficient over the pH range tested. The deriv. (II) and its hydrochloride dissolved rather slowly in the acidic medium, and part of them gradually crystd. out of soln. with increasing pH, due to the low aq. soly. of the neutral form of II. The in vivo absorption studies using beagle dogs revealed that the two salts of I showed excellent oral bioavailability, where the shorter the mean absorption time, the greater the extent of bioavailability.

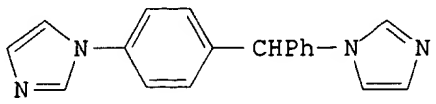
L4 ANSWER 22 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1990:618090 CAPLUS
DN 113:218090
TI Optimization of tablets formulation for Y-20811, a new thromboxane synthetase inhibitor
AU Kino, Shigemi; Shiotsuki, Takako; Gotoh, Mizumi; Oda, Minoru; Ogawa, Kenji; Yokobe, Tetsuo
CS Res. Lab., Yoshitomi Pharm. Ind., Ltd., Fukuoka, 871, Japan
SO Yakuzaigaku (1990), 50(2), 113-18
CODEN: YAKUA2; ISSN: 0372-7629
DT Journal
LA Japanese
GI



I

AB The formulation design of Y-20811(I) for oral dosage form was investigated. Hydroxypropyl Me cellulose 2910 was selected as a binder candidate. The exptl. design technique was applied to optimize the formulation of 50 mg tablets. Dissoln. parameters of the tablets were predicted as a function of the amts. of D-mannitol and NaHCO3. An optimum formulation of the tablets was proposed on the basis of these predictions. The tablets thus obtained showed a significantly facilitated drug-release in the dissoln. test media over the physiol. pH conditions in the gastrointestinal tract.

L4 ANSWER 23 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1990:478279 CAPLUS
DN 113:78279
TI Researches on antibacterial and antifungal agents. XII. Analogs of bifonazole with two imidazole moieties and related azoles
AU Stefancich, Giorgio; Silvestri, Romano; Panico, Salvatore; Artico, Marco; Simonetti, Nicola
CS Dip. Studi Farm., Univ. Roma "La Sapienza", Rome, 00185, Italy
SO Archiv der Pharmazie (Weinheim, Germany) (1990), 323(5), 273-80
CODEN: ARPMAS; ISSN: 0365-6233
DT Journal
LA English
OS CASREACT 113:78279
GI



I

AB Bifonazole analogs, bearing 2 imidazole rings or related azole rings, were prepd. and tested as antifungal agents. E.g., reaction of PhCOC6H4F-p with imidazole/NaH, followed by NaBH4 redn., chlorination with SOCl2, and reaction with imidazole/Et3N gave the diimidazole deriv. I. Also prepd. were tetrazolyl and triazolyl derivs. These analogs possessed only a fraction of the antifungal activity of bifonazole.

L4 ANSWER 24 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1990:429252 CAPLUS
DN 113:29252
TI Pharmaceutical compositions containing thromboxane synthetase inhibitor
IN Oda, Minoru; Kino, Shigemi; Ogawa, Kenji; Shiotsuki, Takako
PA Yoshitomi Pharmaceutical Industries, Ltd., Japan
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8906959	A1	19890810	WO 1989-JP100	19890131
	W: US				
	RW: AT, BE, CH, DE, FR, GB, IT, NL, SE				
	EP 379579	A1	19900801	EP 1989-901749	19890131
	R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE				
	JP 02000704	A2	19900105	JP 1989-24495	19890201
	US 5091191	A	19920225	US 1989-415356	19890925
PRAI	JP 1988-23250		19880203		
	WO 1989-JP100		19890131		

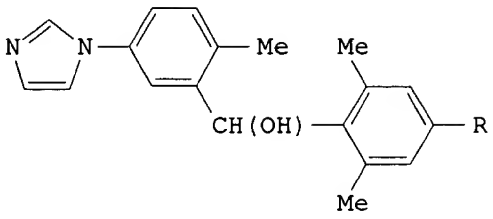
AB A pharmaceutical compn. comprises Na 4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoate (I) or its optical isomer or hydrates having improved releasability and further contains D-mannitol and/or NaHCO3 and a water-sol. high-mol. compd. This compn. can release I irresp. of the pH in digestive tract including stomach. Thus, I 10 and D-mannitol 90% by wt. were mixed with H2O, made into particles, and dried at 50.degree. to give a pharmaceutical powder sol. in the stomach for the treatment of thrombosis and asthma (no pharmacol. data).

L4 ANSWER 25 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1990:400316 CAPLUS
DN 113:316
TI Correlation between pharmacokinetics and pharmacologic effects of a new imidazole thromboxane synthetase inhibitor
AU Iwata, Toshio; Mikashima, Hiroshi; Takamatsu, Rikuo
CS Res. Lab., Yoshitomi Pharm. Ind., Ltd., Fukuoka, 871, Japan
SO Journal of Pharmaceutical Sciences (1990), 79(4), 295-300
CODEN: JPMSAE; ISSN: 0022-3549
DT Journal
LA English
AB A new imidazole deriv., sodium 4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoate dihydrate (I; Y-20811), is a potent selective inhibitor of thromboxane (TX) synthetase and a candidate drug for preventing ischemic circulatory disorders. After oral dosing in

beagle dogs, I persistently inhibited TX prodn., although the elimination of the drug was relatively rapid from plasma. The amt. of drug distributed in platelets was small. However, I was eliminated from platelets very slowly (t1/2 = 41-130 h), the rate of elimination being comparable to the turnover rate of platelets. From the in vitro expts., an obvious pos. correlation was noted between the amt. of the drug bound with TX synthetase in platelets and the inhibition of TX prodn. This correlation suggested that the small amt. of I detected in platelets in vivo was large enough to inhibit TX prodn. From these observations, I is thought to dissoc. extremely slowly from the active sites of TX synthetase. Consequently, the duration of the effect was dependent on the turnover of platelets.

L4 ANSWER 26 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1990:191692 CAPLUS
DN 112:191692
TI Protective effect of Y-20811, a long-lasting thromboxane synthetase inhibitor, on endotoxin shock in rabbits
AU Mikashima, Hiroshi; Muramoto, Yoshito
CS Res. Lab., Yoshitomi Pharm. Ind. Ltd., Yoshitomi, 871, Japan
SO Thrombosis Research (1990), 57(4), 499-505
CODEN: THBRAA; ISSN: 0049-3848
DT Journal
LA English
AB The effect of sodium 4-[.alpha.-hydroxy-5-(imidazolyl)-2-methylbenzyl]-3,5-dimethyl benzoate dihydrate (Y-20811), a selective thromboxane (TX) synthetase inhibitor, on endotoxin shock was investigated in comparison with aspirin. The drugs were orally administered to rabbits at 24 and 1 h before injection of endotoxin (5 mg/kg, i.v.). Y-20811 (1 mg/kg) promoted the recovery of decreased platelet counts and inhibited hypotension induced by endotoxin. It also inhibited the increase in plasma TXB2 and 6-ketoPGF1.alpha.. Aspirin at 30 mg/kg, inhibited hypotension and the increase in both plasma TXB2 and 6-ketoPGF1.alpha. levels, but it failed to inhibit the decrease in platelet counts. In the control group, all rabbits died within 180 min after endotoxin injection, while Y-20811 completely protected animals against death at a dose of 0.3 mg/kg. Aspirin also protected animals against death at a dose of 30 mg/kg, which was, however, about one hundredth as potent as Y-20811. These results indicate that Y-20811 is useful in treating endotoxin shock.

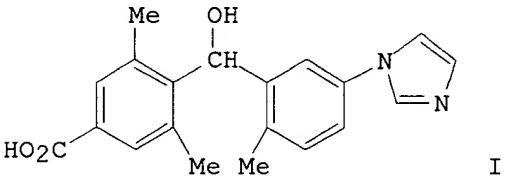
L4 ANSWER 27 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1990:185659 CAPLUS
DN 112:185659
TI Physicochemical properties of new thromboxane synthetase inhibitors, Y-20811 and its related compounds
AU Shiotsuki, Takako; Ogawa, Kenji; Yokobe, Tetsuo
CS Res. Lab., Yoshitomi Pharm. Ind., Ltd., Fukuoka, 871, Japan
SO Yakuzaigaku (1989), 49(3), 227-33
CODEN: YAKUA2; ISSN: 0372-7629
DT Journal
LA Japanese
GI



I, R=CO_2H
II, R=Me

AB Salts of thromboxane synthetase inhibitors I and II, i.e. I Na (III) (Y-20811), I sulfate (IV), I mesylate (V), I-HCl (VI), I-L-lysine salt (VII), II sulfate (VIII), II mesylate (IX), II-HCl (X), and II fumarate (XI) were obtained as crystals. In the course of preformulation studies of I and II, physicochem. properties of their salts were evaluated. VI, VII, X and XI were unstable in stability tests. V and IX had unfavorable behavior in dissoln. tests. III, IV and VIII were free from such problems. These salts tended to form supersatd. solns. in the dissoln. test media. The mechanisms of the supersatn. of III and IV in the test media were investigated. It was proposed that their supersatn. involves accelerated dissoln. through the diffusion layers and self-buffering effects or hydrations.

L4 ANSWER 28 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1990:69359 CAPLUS
DN 112:69359
TI Pharmacokinetics of sodium 4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoate (Y 20811), a new thromboxane synthetase inhibitor. II. Pharmacokinetics of intact drug and main metabolite in dog
AU Iwata, Toshio; Mikashima, Hiroshi; Isobe, Masao; Takamatsu, Rikuo; Yokobe, Tetsuo
CS Res. Lab., Yoshitomi Pharm. Ind. Ltd., Fukuoka, 871, Japan
SO Yakugaku Zasshi (1989), 109(11), 853-7
CODEN: YKKZAJ; ISSN: 0031-6903
DT Journal
LA Japanese
GI



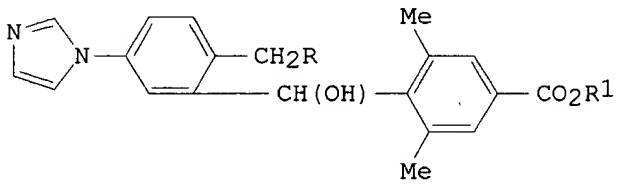
I

AB The pharmacokinetics of Y 20811 (I-Na) in the beagle dog was investigated after oral and i.v. administration. After the administration of I-Na at 3 mg/kg (oral), 70.9% of the dose was absorbed, and the max. plasma concn. of I was obsd. at 0.33 h. After oral administration, the area under the plasma concn.-time curve of I increased almost linearly in proportion to the dose. The hydroxymethyl metabolite, II, was also detected in the plasma, but the concn. of II was lower than I. After the administration at 3 mg/kg (oral), 27.7 and 3.8% of the dose were recovered as I and II, resp., in the urine, and 32.2 and 30.1% recovered as I and II in the feces. Therefore, 93.8% of the dose was totally recovered within 5 days. The inhibitory effect of II on the aggregation of rabbit platelets was studied in vitro. This metabolite showed only one sixth activity of I-Na.

Thus, the inhibitory effect on the platelet aggregation of II is considered to be almost negligible in the beagle dog administered with I-Na.

L4 ANSWER 29 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1990:20938 CAPLUS
DN 112:20938
TI Direct separation of enantiomers by reversed-phase high performance liquid chromatography on cellulose tris(3,5-dimethylphenylcarbamate)
AU Ikeda, Kuniki; Hamasaki, Toshio; Kohno, Hisashi; Ogawa, Takayuki; Matsumoto, Takashi; Sakai, Junichi
CS Res. Lab., Yoshitomi Pharm. Ind., Ltd., Fukuoka, 871, Japan
SO Chemistry Letters (1989), (6), 1089-90
CODEN: CMLTAG; ISSN: 0366-7022
DT Journal
LA English
AB Various types of enantiomeric drugs, e.g. Y-20811, were optically sepd. by reversed-phase high performance liq. chromatog. using cellulose tris(3,5-dimethylphenylcarbamate) as a chiral stationary phase.

L4 ANSWER 30 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1990:15886 CAPLUS
DN 112:15886
TI Pharmacokinetics of sodium 4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoate (Y-20811), a new thromboxane synthetase inhibitor. I. Isolation and structure elucidation of urinary metabolite in dogs.
AU Iwata, Toshio; Tsuruda, Mineo; Demizu, Kenichi; Isobe, Masao; Takamatsu, Rikuo; Yokobe, Tetsuo
CS Res. Lab., Yoshitomi Pharm. Ind. Ltd., Fukuoka, 871, Japan
SO Yakugaku Zasshi (1989), 109(9), 636-41
CODEN: YKKZAJ; ISSN: 0031-6903
DT Journal
LA Japanese
GI

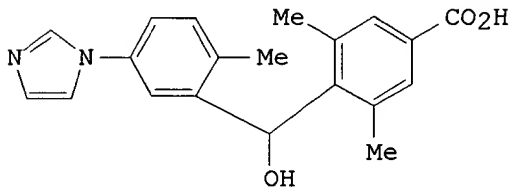


I, R=H, R^1=Na
II, R=OH, R^1=H

AB The urinary metabolites of Y-20811 (I) in dogs were investigated. The main metabolite was isolated by HPLC and subsequent preparative TLC. The structure of this metabolite was established as 4-[.alpha.-hydroxy-2-hydroxymethyl-5-(1-imidazolyl)benzyl]-3,5-dimethylbenzoic acid (II) on the basis of spectral analyses and confirmed by its total synthesis.

L4 ANSWER 31 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1989:614429 CAPLUS
DN 111:214429
TI Thromboxane synthetase inhibitors. II. Optical resolution of 4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoic acid
AU Tsuruda, Mineo; Shiotsuki, Takako; Matsumoto, Takashi; Oe, Takanori
CS Res. Lab., Yoshitomi Pharm. Ind., Ltd., Yoshitomi, 871, Japan

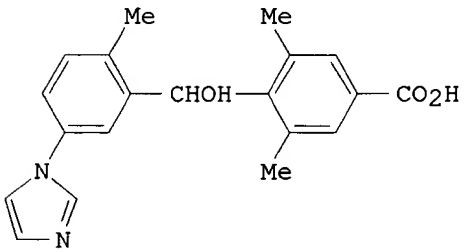
SO Yakugaku Zasshi (1989), 109(1), 26-32
CODEN: YKKZAJ; ISSN: 0031-6903
DT Journal
LA Japanese
OS CASREACT 111:214429
GI



I

AB The optical resoln. of racemic 4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoic acid (dl-I), a new potent and long lasting thromboxane synthetase inhibitor, was investigated. (S)-3-(3,5-Dinitrobenzoylthio)-2-methylpropionyl group was introduced to .alpha.-hydroxy moiety of Me ester of dl-I by three steps of reaction to give the corresponding ester compd. Then, two diastereomers of esters, were sepd. by column chromatog. using on silica gel. Alk. hydrolysis of ester enantiomers, followed by reactions with NaOEt gave optically pure sodium salts of (-)-I and (+)-I, resp. The separative detn. methods for the diastereomers of esters, and for the enantiomers of the sodium salts of dl-I by high performance liq. chromatog. were also established.

L4 ANSWER 32 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1989:534040 CAPLUS
DN 111:134040
TI Thromboxane synthetase inhibitors. I. Synthesis of some imidazolylarylmethanols and their inhibitory activity on platelet aggregation
AU Tsuruda, Mineo; Mikashima, Hiroshi; Oe, Takanori; Kawasaki, Kazuyuki; Setoguchi, Shinro; Naka, Yoichi; Tahara, Tetsuya
CS Res. Lab., Yoshitomi Pharm. Ind., Ltd., Yoshitomi, 871, Japan
SO Yakugaku Zasshi (1989), 109(1), 33-45
CODEN: YKKZAJ; ISSN: 0031-6903
DT Journal
LA Japanese
OS CASREACT 111:134040
GI



I

AB Several imidazolylpyridinemethanols and imidazolylbenzenemethanols were

prepd. and evaluated for inhibitory activity against arachidonic acid-induced platelet aggregation. The result shows that the arylmethanol moiety is essential for the activity and may correspond to the 15-OH group of prostaglandin H2. Among the compds. tested, imidazolylbenzyl alc. deriv. I was found to have a potent inhibitory activity and a long duration of action. Structure-activity relationships are also discussed briefly.

L4 ANSWER 33 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1989:18546 CAPLUS
DN 110:18546
TI Imidazole derivatives as immunostimulants
IN Kudome, Masao; Mikashima, Hiroshi; Tsuruta, Mineo
PA Yoshitomi Pharmaceutical Industries, Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 11 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

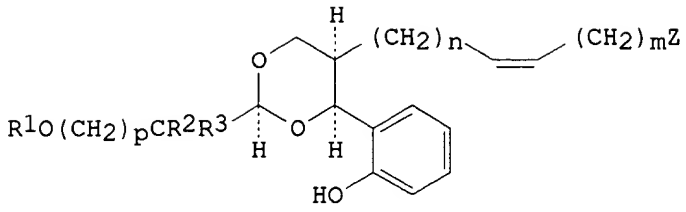
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 63119425	A2	19880524	JP 1986-266455	19861107
PRAI JP 1986-266455		19861107		

OS MARPAT 110:18546
GI For diagram(s), see printed CA Issue.
AB The title compds. I [R1 = H, lower alkyl; R2 = H, halo, lower alkyl, alkoxy, etc.; ring A = benzene ring, pyridine ring, furan ring, thiophene ring; XY = :O, or one of X and Y is H, lower alkyl, the other is OH; Z = alkyl, cycloalkyl, aryl, heteroaryl] are tested for immunostimulating activities. In a test using mice dosed with sheep erythrocytes and cyclophosphamide, Na 4-[.alpha.-hydroxy-2-methyl-5-(1-imidazolyl)benzyl]-3,5-dimethylbenzoate.2H2O caused an immunorestorative response of 359% (control = 100%).

L4 ANSWER 34 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1988:637035 CAPLUS
DN 109:237035
TI Therapeutic agents containing TXA2 antagonists and TXA2 synthesis inhibitors
IN Smithers, Michael James
PA Imperial Chemical Industries PLC, UK
SO Eur. Pat. Appl., 24 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 266979	A2	19880511	EP 1987-309634	19871030
EP 266979	A3	19891102		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 8707885	A	19880629	ZA 1987-7885	19871020
AU 8780551	A1	19880505	AU 1987-80551	19871030
DK 8705766	A	19880505	DK 1987-5766	19871103
US 4925869	A	19900515	US 1987-118227	19871103
JP 63130531	A2	19880602	JP 1987-277554	19871104
PRAI GB 1986-26296		19861104		

OS MARPAT 109:237035
GI



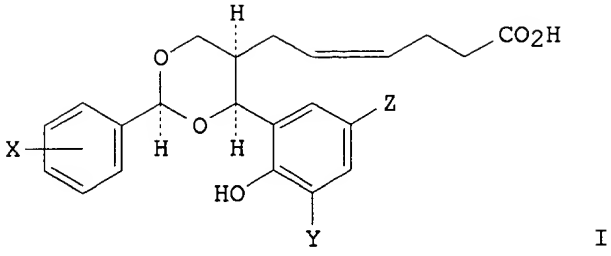
I

AB A TXA2 antagonist dioxane ether [I; R1 = alkyl, cycloalkyl, cycloalkylalkyl, (substituted) Ph, (substituted) phenylalkyl; R2, R3 = H, C1-4 alkyl, (alkyl-substituted) C3-6 polymethylene; Z = CO2H, 1H-tetrazol-5-yl; m = 2-4; n = 1, 2; p = 0-2] and a TXA2 formation inhibitor are useful together for treatment of disorders involving TXA2 and/or other prostanoid contractile substances. I (R1 = Ph, R2 = R3 = Me, Z = CO2H, m = 2, n = 1, p = 0) (II) was prepd. from 4-(o-methoxyphenyl)-2,2-dimethyl-1,3-dioxan-cis-5-ylacetaldehyde by Wittig reaction with HO2CCH2CH2PPh3Br and KOCMe3 to form the 4(Z)-dioxan-5-ylhexenoic acid deriv., transketalization with 2-methyl-2-phenoxypropionaldehyde [prepd. by redn. of PhCMe2CO2Me with (Me2CHCH2)2AlH], and removal of the methoxy Me group with Ph2PLi. An aerosol was prepd. from a TXA2 antagonist (e.g. II) 0.1, a TXA2 synthesis inhibitor (e.g. dazoxiben or CV4151) 0.1, sorbitan trioleate 0.27, CCl3F 70.0, CCl2F2 280.0, and C2Cl2F4 1094.0 mg/mL. Human blood platelet aggregation in response to arachidonic acid was completely inhibited by a combination of II (10-9M) and dazoxiben (10-4M), whereas either agent alone was ineffective.

L4 ANSWER 35 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1988:631037 CAPLUS
DN 109:231037
TI Pharmaceutical compositions
IN Brewster, Andrew George; Brown, George Robert; Smithers, Michael James
PA Imperial Chemical Industries PLC, UK
SO Eur. Pat. Appl., 30 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 266980	A2	19880511	EP 1987-309635	19871030
	EP 266980	A3	19891108		
	EP 266980	B1	19921028		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	ZA 8707886	A	19880629	ZA 1987-7886	19871020
	IL 84261	A1	19911215	IL 1987-84261	19871023
	AT 81774	E	19921115	AT 1987-309635	19871030
	ES 2052581	T3	19940716	ES 1987-309635	19871030
	DK 8705768	A	19880505	DK 1987-5768	19871103
	US 4908380	A	19900313	US 1987-118226	19871103
	CA 1308660	A1	19921013	CA 1987-550880	19871103
	AU 8780698	A1	19880505	AU 1987-80698	19871104
	AU 608546	B2	19910411		
	JP 63130532	A2	19880602	JP 1987-277555	19871104
PRAI	GB 1986-26297		19861104		
	EP 1987-309635		19871030		

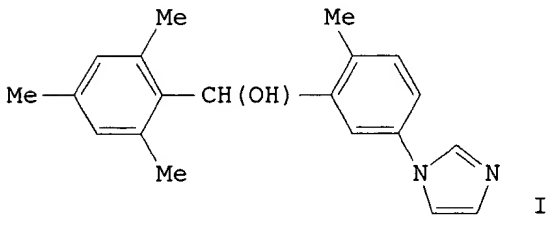
OS MARPAT 109:231037
GI



I

AB A TXA2 antagonist 2,4-diphenyl-1,3-dioxane deriv. I (X = F, Cl, Br, F3C, cyano, MeO, O2N; 1 of Y, Z = H, F and the other = H) and a TXA2 formation inhibitor are useful together for treatment of disorders involving TXA2 and/or other prostanoid contractile substances. I (X = 2-cyano; Y = Z = H) (II) was prepd. from [4-(o-methoxyphenyl)-2,2-dimethyl-1,3-dioxan-cis-5-yl]acetaldehyde by Wittig reaction with HO2C(CH2)3PPh3Br and KOCMe3 to form the 4(Z)-dioxan-5-ylhexenoic acid deriv., followed by transketalization with o-cyanobenzaldehyde, and removal of the methoxy Me group with NaH in the presence of EtSH. Human blood platelet aggregation in response to arachidonic acid was 89.9% inhibited by a combination of I (X = 2-Cl; Y = Z = H) (10-9M) and dazoxiben (10-5M), compared to 2.2 and 4.5%, resp., for each agent used sep. A capsule was prepd. contg. a TXA2 antagonist (e.g. II) 5, a TXA2 synthetase inhibitor (e.g. dazoxiben) 5, lactose 488.5, and Mg stearate 1.5 mg.

L4 ANSWER 36 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1987:611652 CAPLUS
DN 107:211652
TI Antinephritic effect of Y-19018, a thromboxane A synthetase inhibitor, on crescentic-type anti-GBM nephritis in rats
AU Suzuki, Yoshio; Tsukushi, Yoshihito; Ito, Mikio; Nagamatsu, Tadashi
CS Fac. Pharm., Meijo Univ., Nagoya, 468, Japan
SO Japanese Journal of Pharmacology (1987), 45(2), 177-85
CODEN: JJPAAZ; ISSN: 0021-5198
DT Journal
LA English
GI



I

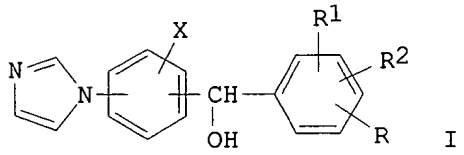
AB The antinephritic effect of Y-19018 (I) a thoromboxane A synthetase inhibitor, on crescentic-type anti-glomerular basement membrane (anti-GBM) nephritis in rats was studied. Male Sprague Dawley rats were immunized with rabbit .gamma.-globulin in Freund's complete adjuvant following i.v.

injection of anti-GBM serum. Y-19018 at a dose of 0.3 and 3.0 mg/kg was given orally to rats from the day after the injection of anti-GBM serum (day 1) to day 39. Y-19018, 3.0 mg/kg, inhibited both urinary protein excretion (30.6%) on day 19 and plasma cholesterol (39.8%) on day 15. Moreover, light microscopy demonstrated that this drug at both doses remarkably prevented histol. involvement of the glomeruli on day 40 in a dose-dependent manner. In the blood obtained from nephritic rats, platelet aggregation was increased. Y-19018 suppressed (48.7%) the hyperaggregability of platelets on day 40 at a high dose, although the suppression of platelet aggregation was not in a dose-dependent manner. Apparently, Y-19018 shoiws beneficial effects on crescentic-type anti-GBM nephritis and may exert its action partly through inhibition of glomerular TXA2.

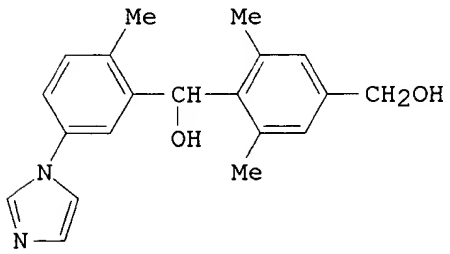
L4 ANSWER 37 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1987:515589 CAPLUS
DN 107:115589
TI 5-(Imidazol-1-yl)-.alpha.-(2,6-dimethylphenyl)benzenemethanol derivatives as drugs
IN Tsuruta, Mineo; Ooe, Takanori; Kawasaki, Kazuyuki; Mikashima, Hiroshi; Yasuda, Hiroshi
PA Yoshitomi Pharmaceutical Industries, Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 62000470	A2	19870106	JP 1985-139952	19850625
	JP 05074589	B4	19931018		
PRAI	JP 1985-139952		19850625		

OS CASREACT 107:115589
GI



I



II

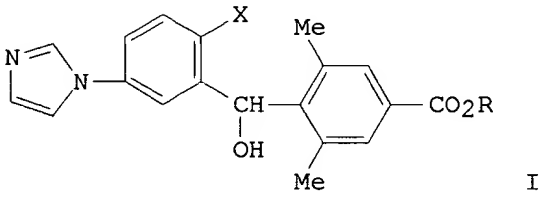
AB The title compds. [I; R = CHO, CHR3R4 [R3 = H, alkyl; R4 = OH, alkoxy, acyloxy, (unsubstituted PhO], ZNR5R6 (Z = CO, CH2, alkylmethylene; R5, R6 = H, acyl, hydroxyalkyl, carboxyalkyl, 1-substituted piperidyl or NR5R6 = heterocyclyl); R1R2 = H, alkyl; X = H, halo, alkyl, alkoxy], useful as

inhibitors of thromboxane A2 synthesis and blood platelet aggregation (no data), were prepd. A mixt. of 5-iodo-2,2',6'-trimethyl-4'-(ethoxycarbonyl)benzophenone and imidazole contg. K2CO3, Cu powder, and KF was heated at 140.degree. for 4 h to give 5-(imidazol-1-yl)-2,2',6'-trimethyl-4'-(ethoxycarbonylbenzophenone, which was reduced by LiAlH4 to give an .alpha.-phenylbenzyl alc. deriv. II.

L4 ANSWER 38 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1987:213946 CAPLUS
DN 106:213946
TI 4-(.alpha.-Hydroxy-3-imidazol-1-ylbenzyl)benzoates as blood platelet aggregation inhibitors
IN Tsuruta, Mineo; Oe, Takanori; Kawasaki, Kazuyuki; Mikashima, Hiroshi; Yasuda, Hiroshi
PA Yoshitomi Pharmaceutical Industries, Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 61282366	A2	19861212	JP 1985-124617	19850607
JP 05029031	B4	19930428		
PRAI JP 1985-124617		19850607		

OS CASREACT 106:213946
GI



I

AB The title compds. (I; X = halo, alkyl, alkoxy; R = H, alkyl; when X = alkyl, R = alkyl) and their pharmaceutically acceptable salts and/or hydrates, inhibiting blood platelet aggregation and biosynthesis of thromboxane A2, thereby useful for prophylaxis and treatment of asthma, heart ailments, high blood pressure, nephritis, etc. (no data), were prepd. Thus, a mixt. of 4-(.alpha.-hydroxy-2-chloro-5-iodobenzyl)-3,5-dimethylbenzoic acid, imidazole, K2CO3, KF and Cu powder in DMF was heated at 135-140.degree. for 30 h to give I (X = Cl, R = H).

L4 ANSWER 39 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1987:207671 CAPLUS
DN 106:207671
TI .alpha.-(2,4,6-Trimethylphenyl)-2-methyl-5-(1-imidazolyl)benzenemethanol or its pharmaceutically acceptable salt as therapeutic agent for nephritis
IN Suzuki, Yoshio
PA Yoshitomi Pharmaceutical Industries, Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

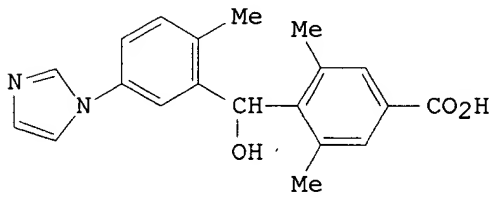
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 62010014	A2	19870119	JP 1985-147210	19850704
PRAI	JP 1985-147210		19850704		

AB .alpha.-(2,4,6-Trimethylphenyl)-2-methyl-5-(1-imidazolyl)benzenemethanol (I) or its pharmacol. acceptable salts are effective in treating nephritis. Male Sprague-Dawley rats were treated i.v. with anti-glomerular basement membrane antiserum, followed by injection of rabbit .gamma.-globulin in complete Freund's adjuvant into the footpad to induce nephritis. I (0.3 or 3.0 mg/kg, orally) was administered to the rats from the 2nd day of i.v. antiserum injection, and the kidney was isolated on day 41 for microscopic examn. Pathol. changes were markedly reduced compared to control animals.

L4 ANSWER 40 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1987:138446 CAPLUS
DN 106:138446
TI 4-[.alpha.-Hydroxy-2-methyl-5-(imidazol-1-yl)benzyl]-3,5-dimethylbenzoic acid
IN Tsuruta, Mineo; Oe, Takanori; Kawasaki, Kazuyuki; Mikashima, Hiroshi; Yasuda, Hiroshi
PA Yoshitomi Pharmaceutical Industries, Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 61277670	A2	19861208	JP 1985-121220	19850603
	JP 05041143	B4	19930622		
	US 4661603	A	19870428	US 1986-823633	19860129
PRAI	JP 1982-34365		19820303		
	US 1983-556231		19831031		
	JP 1985-121220		19850603		

OS CASREACT 106:138446
GI

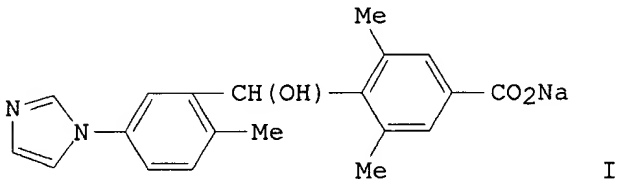


I

AB The title compd. (I), useful as cardiovascular agents, for treatment of asthma, nephritis, and for prevention of cancer metastasis, were prepd. Thus, a mixt. of 4-(2-methyl-5-iodobenzoyl)-3,5-dimethylbenzoic acid and imidazole in DMF contg. K2CO3, KF, and Cu powder was heated at 135.degree. for 24 h to give, after treatment with Na2S.cntdot.3H2O and acidification, 4-[2-methyl-5-(imidazol-1-yl)benzoyl]-3,5-dimethylbenzoic acid whose redn. with NaBH4 in aq. NaOH at 70-75.degree. for 3 h gave, after acidification, I. This at 2.3 .times. 10-8 and >10-4 M in vitro inhibited by 50% thromboxane synthetase in human blood platelet microsomes and

cyclooxygenase in bovine seminal vesicle microsomes resp.

L4 ANSWER 41 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1986:545895 CAPLUS
DN 105:145895
TI Effects of Y-20811, a long-lasting thromboxane synthetase inhibitor, on thromboxane production and platelet function
AU Mikashima, Hiroshi; Ochi, Hiroshi; Muramoto, Yoshito; Yasuda, Hiroshi; Tsuruta, Mineo; Maruyama, Yutaka
CS Res. Lab., Yoshitomi Pharm. Ind. Ltd., Fukuoka, 871, Japan
SO Thrombosis Research (1986), 43(4), 455-68
CODEN: THBRAA; ISSN: 0049-3848
DT Journal
LA English
GI



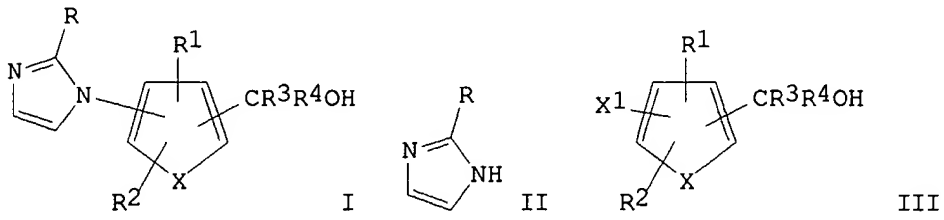
I

AB Effects of a new imidazole deriv., Y-20811 (I) [**104363-98-6**], on thromboxane (TX) prodn. and platelet aggregation were investigated. Y-20811 inhibited TX synthetase [61276-89-9] and platelet aggregation induced by arachidonic acid (AA) in human, guinea pig and rabbit platelets in vitro. Administered orally to rabbits, Y-20811 at 1 mg/kg decreased serum TXB2 concomitant with increasing 6-keto PGF1.alpha. and at 3 mg/kg inhibited AA-induced platelet aggregation, in both cases for at least 48 h. Y-20811 (0.3 mg/kg/day) administered to rabbits for 7 days decreased serum TXB2 levels by 50-90% during the medication, and these levels were restored to initial values 3 days after withdrawal of the drug. At 1 mg/kg, Y-20811 protected rabbits against death induced by AA (2 mg/kg). These results indicate that Y-20811 is a selective and long-lasting TX synthetase inhibitor and an antiaggregation agent useful in preventing thrombotic disorders.

L4 ANSWER 42 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1986:109631 CAPLUS
DN 104:109631
TI Imidazole derivatives
IN Tsuruta, Mineo; Oe, Takanori; Kawasaki, Kazuyuki; Mikashima, Hiroshi; Yasuda, Hiroshi
PA Yoshitomi Pharmaceutical Industries, Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 60142965	A2	19850729	JP 1983-163951	19830905
	JP 04015781	B4	19920319		
PRAI	JP 1983-163951		19830905		

OS CASREACT 104:109631
GI

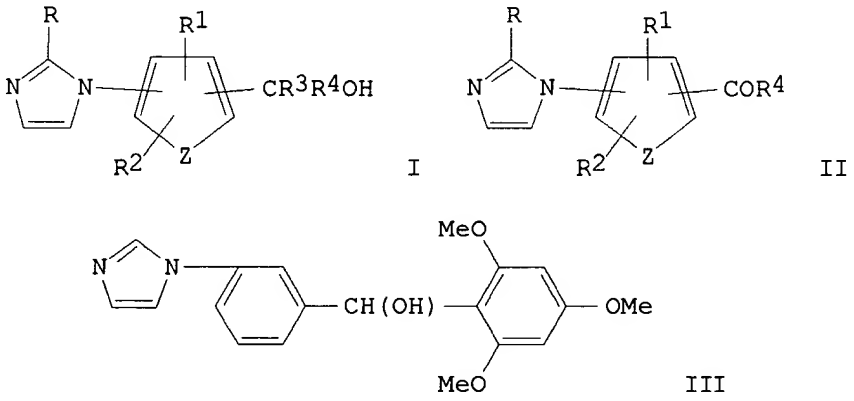


AB Title compds. I [R, R3 = H, lower alkyl; R1, R2 = H, halo, OH, lower alkyl, lower alkoxy, aralkyloxy, NO2, NH2; X = O, S, CH:CH, CH:N; R4 = (substituted) aryl] and their acid salts, useful as thromboxane A2 synthesis inhibitors, platelet aggregation inhibitors, and vasodilators, (no data), were prepd. by treating imidazoles II with alcs. III (X1 = halo). Thus, refluxing 2 g imidazole II (R = H) with 10.7 g 2,5-ClIC6H3CH(OH)C6H2Me3-2,4,6 in DMF contg. 4.3 g K2CO3, 0.3 g Cu, and 0.3 g KF for 4.5 h gave 7.7 g 2,5-ClQC6H3CH(OH)C6H2Me3-2,4,6 (Q = 1H-imidazol-1-yl).

L4 ANSWER 43 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1985:615282 CAPLUS
DN 103:215282
TI Imidazole derivatives
PA Yoshitomi Pharmaceutical Industries, Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 60034952	A2	19850222	JP 1983-53333	19830328
PRAI JP 1983-53333		19830328		

OS CASREACT 103:215282
GI



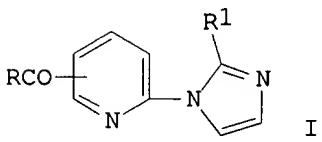
AB Sixty-three imidazole alc. derivs. I [R, R3 = H, alkyl; R1, R2 = H, halo,

OH, alkyl, etc.; Z = O, S, CH:CH, CH:N; R4 = aryl, (un)substituted thienyl, pyridyl, furyl] were prepd., e.g., by redn. of ketones II. Blood platelet aggregation inhibitory data of I were shown using rabbit plasma (68-100 % inhibition at 10 mg/kg orally in rats) with LD50 >1000 mg/kg. Thus, 3.4 g NaHB4 in H2O was added to 16 g 3-(1-imidazolyl)-2',4',6'-trimethylbenzophenone in EtOH and the mixt. stirred 20 h at 56.degree. to give 13.6 g .alpha.-(2,4,6-trimethylphenyl)-3-(1-imidazolyl)benzenemethanol.

L4 ANSWER 44 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1985:62232 CAPLUS
DN 102:62232
TI 2-(1-Imidazolyl)-3(or 5)-aroylpyridines
PA Yoshitomi Pharmaceutical Industries, Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 59139379	A2	19840810	JP 1983-13201	19830129
	JP 01007074	B4	19890207		
PRAI	JP 1983-13201		19830129		

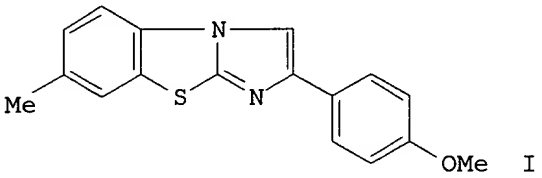
GI



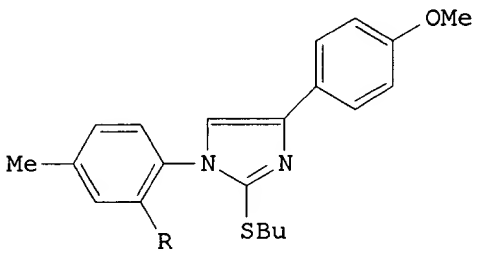
I

AB Twenty-nine title pyridines (I) (R = Ph, 4-chlorophenyl, 5-methyl-2-hydroxyphenyl, 2-methyl-3-indolyl, 6-methoxy-2-naphthyl, etc.; R1 = H, Me, Et2NCH2), having analgesic, antiinflammatory, and other activities (no data), were prepd. Thus, 29.6 g imidazole were stirred with NaH in DMF 1 h, then treated with 50 g 2-chloro-3-cyanopyridine to give 50 g 2-(1-imidazolyl)-3-cyanopyridine, which (20 g) was stirred with PhMgBr in Et2O-C6H6 and hydrolyzed to give 16.7 g I (R = 3-Ph, R1 = H).

L4 ANSWER 45 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1984:472665 CAPLUS
DN 101:72665
TI Imidazo[2,1-b]benzothiazole. Nucleophilic substitution reaction on sulfur by n-butyllithium
AU Mase, Toshiyasu; Murase, Kiyoshi
CS Cent. Res. Lab., Yamanouchi Pharm. Co., Ltd., Tokyo, 174, Japan
SO Heterocycles (1984), 22(5), 1013-15
CODEN: HTCYAM; ISSN: 0385-5414
DT Journal
LA English
OS CASREACT 101:72665
GI



I



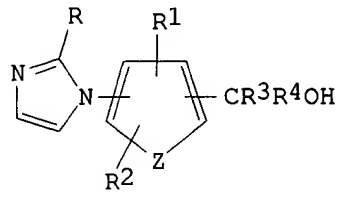
II

AB Imidazobenzothiazole deriv. I was converted to 1-phenyl-2-(butylthio)imidazoles II [R = CO2H, H, 4-MeC6H4CH(OH)]. I was treated with BuLi in THF, and the organolithium intermediate was quenched with 4-MeC6H4CHO to give II [R = 4-MeC6H4CH(OH)].

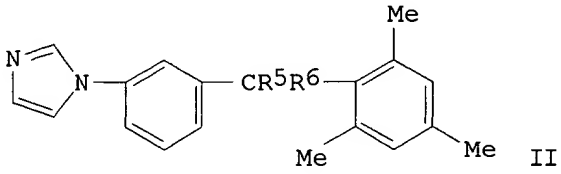
L4 ANSWER 46 OF 58 CAPLUS COPYRIGHT 2003 ACS
AN 1984:103343 CAPLUS
DN 100:103343
TI Imidazole derivatives
IN Tsuruda, Mineo; Oe, Takanori; Kawasaki, Kazuyuki; Mikashima, Hiroshi; Yasuda, Hiroshi
PA Yoshitomi Pharmaceutical Industries, Ltd. , Japan
SO PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 8303096	A1	19830915	WO 1983-JP60	19830228
	W: US				
	RW: AT, BE, DE, FR, GB, NL, SE				
	JP 58150566	A2	19830907	JP 1982-34365	19820303
	JP 03016348	B4	19910305		
	EP 110996	A1	19840620	EP 1983-900734	19830228
	EP 110996	B1	19860903		
	R: AT, BE, DE, FR, GB, NL, SE				
	AT 21895	E	19860915	AT 1983-900734	19830228
	CA 1244032	A1	19881101	CA 1983-435834	19830831
	US 4581369	A	19860408	US 1983-556231	19831031
PRAI	JP 1982-34365		19820303		
	EP 1983-900734		19830228		
	WO 1983-JP60		19830228		

OS CASREACT 100:103343
GI



I



II

AB Seventy imidazole derivs. I (R, R3 = H, alkyl; R1, R2 = H, halo, alkyl, HO, alkoxy, aryloxy, O2N, H2N; R4 = aryl, thienyl, pyridyl, furyl; Z = O, S, CH:CH, CH:N), effective blood platelet aggregation inhibitors at 10 mg/kg and cyclooxygenase inhibitors at 2.3 .times. 10-6 to 1.8 .times. 10-7 mol, were prepd. Thus, 3.4 g NaBH4 in H2O was added to a suspension of 16 g benzophenone II (R5R6 = O) in EtOH and stirred 20 h at 56.degree. to give 13.6 g alc. deriv. (II; R5 = H, R6 = HO).

L4 ANSWER 47 OF 58 USPATFULL
AN 2003:72018 USPATFULL
TI Thromboxane inhibitors, compositions and methods of use
IN Tejada, Inigo Saenz de, Madrid, SPAIN
PI US 2003050305 A1 20030313
AI US 2002-285620 A1 20021101 (10)
RLI Continuation of Ser. No. WO 2001-US16318, filed on 22 May 2001, PENDING
PRAI US 2000-205536P 20000522 (60)
DT Utility
FS APPLICATION
LREP EDWARD D GRIEFF, HALE & DORR LLP, 1455 PENNSYLVANIA AVE, NW, WASHINGTON, DC, 20004
CLMN Number of Claims: 73
ECL Exemplary Claim: 1
DRWN 8 Drawing Page(s)
LN.CNT 2750
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention describes methods for treating or preventing sexual dysfunctions in males and females, and for enhancing sexual responses in males and females by administering a therapeutically effective amount of at least one thromboxane inhibitor, and, optionally, at least one compound that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase, and/or at least one vasoactive agent. The male or female may preferably be diabetic. The present invention also provides novel compositions comprising at least one thromboxane inhibitor, and, at least one compound that donates, transfers or releases nitric oxide, elevates endogenous levels of endothelium-derived relaxing factor, stimulates endogenous synthesis of nitric oxide or is a substrate for nitric oxide synthase, and, optionally, at least one therapeutic agent, such as, vasoactive agents, nonsteroidal antiinflanmmatory compounds (NSAIDs), selective cyclooxygenase-2 (COX-2) inhibitors, anticoagulants, angiotensin converting enzymes (ACE) inhibitors, angiotensin II receptor antagonists, renin inhibitors, and mixtures thereof. The present

invention also provides methods for treating or preventing ischemic heart disorders, myocardial infarction, angina pectoris, stroke, migraine, cerebral hemorrhage, cardiac fatalities, transient ischaemic attacks, complications following organ transplants, coronary artery bypasses, angioplasty, endarterectomy, atherosclerosis, pulmonary embolism, bronchial asthma, bronchitis, pneumonia, circulatory shock of various organs, nephritis, graft rejection, cancerous metastases, pregnancy-induced hypertension, preeclampsia, eclampsia, thrombotic and thromboembolic disorders, intrauterine growth, gastrointestinal disorders, renal diseases and disorders, disorders resulting from elevated uric acid levels and dysmenorrhea, and for inhibiting platelet aggregation or platelet adhesion or relaxing smooth muscles.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 48 OF 58 USPATFULL
AN 2002:301648 USPATFULL
TI Method for prophylaxis and treatment of diabetic complications with 4[alpha-hydroxy-2-methyl-5-(1-imidazolyl)benzyl]-3,5-dimethylbenzoic acid and derivatives
IN Hayashi, Yoshiharu, Iruma-shi, JAPAN
Goto, Nobuharu, Iruma-shi, JAPAN
PI US 2002169194 A1 20021114
AI US 2002-80660 A1 20020225 (10)
RLI Continuation of Ser. No. US 2001-850000, filed on 8 May 2001, ABANDONED
Division of Ser. No. US 2000-498481, filed on 4 Feb 2000, PATENTED
Division of Ser. No. US 1998-91993, filed on 26 Jun 1998, PATENTED A 371 of International Ser. No. WO 1996-JP3776, filed on 24 Dec 1996, UNKNOWN
PRAI JP 1995-340161 19951227
DT Utility
FS APPLICATION
LREP WENDEROTH, LIND & PONACK, L.L.P., 2033 K STREET N. W., SUITE 800, WASHINGTON, DC, 20006-1021
CLMN Number of Claims: 24
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 653
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to an agent for the prophylaxis and treatment of diabetic complications comprising, as an active ingredient, 4-[.alpha.-hydroxy-2-methyl-5(1-imidazolyl)benzyl]-3,5-dimethylbenzoic acid, an optically active compound thereof or a pharmaceutically acceptable salt thereof. The present invention further relates to a method for the prophylaxis and treatment of diabetic complications comprising administering an effective amount of this compound. The medicament of the present invention is useful for the prophylas and treatment of diabetic complications, namely, diabetic neuropathy, nephropathy, ophthalmopathy, arteriosclerosis and the like. The action of the drug is long-lasting for very small doses and a single administration a day is sufficient

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 49 OF 58 USPATFULL
AN 2001:194442 USPATFULL
TI Method for prophylaxis and treatment of diabetic complications with 4[alpha-hydroxy-2-methyl-5(1-imidazolyl)benzyl]-3,5-dimethylbenzoic acid and derivatives
IN Hayashi, Yoshiharu, Iruma-shi, Japan
Goto, Nobuharu, Iruma-shi, Japan

09/979,509

PI US 2001036957 A1 20011101
AI US 2001-850000 A1 20010508 (9)
RLI Division of Ser. No. US 2000-498481, filed on 4 Feb 2000, GRANTED, Pat. No. US 6258834 Division of Ser. No. US 1998-91993, filed on 26 Jun 1998, GRANTED, Pat. No. US 6060496 A 371 of International Ser. No. WO 1996-JP3776, filed on 24 Dec 1996, UNKNOWN
PRAI JP 1995-340161 19951227
DT Utility
FS APPLICATION
LREP WENDEROTH, LIND & PONACK, L.L.P., 2033 K STREET N. W., SUITE 800, WASHINGTON, DC, 20006-1021
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 629
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to an agent for the prophylaxis and treatment of diabetic complications comprising, as an active ingredient, 4-[.alpha.-hydroxy-2-methyl-5-(1-imidazolyl)benzyl]-3,5-dimethylbenzoic acid, an optically active compound thereof or a pharmaceutically acceptable salt thereof. The present invention fuher relates to a method for the prophylaxis and treatment of diabetic complications comprising administering an effective amount of this compound. The medicament of the present invention is useful for the prophylaxis and treatment of diabetic complications, namely, diabetic neuropathy, nephropathy, ophthalimopathy, arteriosclerosis and the like. The action of the drug is long-lasting for very small doses and a single administration a day is sufficient.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 50 OF 58 USPATFULL
AN 2001:107916 USPATFULL
TI Method for prophylaxis and treatment of diabetic complications with 4[.alpha.-hydroxy-2-methyl-5-(1-imidazolyl)benzyl]-3,5-dimethylbenzoic acid and derivatives
IN Hayashi, Yoshiharu, Iruma, Japan
Goto, Nobuharu, Iruma, Japan
PA Welfide Corporation, Osaka, Japan (non-U.S. corporation)
PI US 6258834 B1 20010710
AI US 2000-498481 20000204 (9)
RLI Division of Ser. No. US 91993, now patented, Pat. No. US 6060496
PRAI JP 1995-340161 19951227
DT Utility
FS GRANTED
EXNAM Primary Examiner: Higel, Floyd D.
LREP Wenderoth, Lind & Ponack, L.L.P.
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 601
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to an agent for the prophylaxis and treatment of diabetic complications comprising, as an active ingredient, 4-[.alpha.-hydroxy-2-methyl-5-(1-imidazolyl)benzyl]-3,5-dimethylbenzoic acid, an optically active compound thereof or a pharmaceutically acceptable salt thereof. The present invention further relates to a method for the prophylaxis and treatment of diabetic complications comprising administering an effective amount of this compound. The medicament of the present invention is useful for the prophylaxis and

treatment of diabetic complications, namely, diabetic neuropathy, nephropathy, ophthalmopathy, arteriosclerosis and the like. The action of the drug is long-lasting for very small doses and a single administration a day is sufficient.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 51 OF 58 USPATFULL
AN 2000:174847 USPATFULL
TI Production method of optically active imidazole compound, synthetic intermediate therefor and production method thereof
IN Kawasaki, Kazuyuki, Chikujo-gun, Japan
Kobayashi, Haruhito, Chikujo-gun, Japan
Ehara, Syuji, Chikujo-gun, Japan
Sato, Hideaki, Chikujo-gun, Japan
PA Yoshitomi Pharmaceutical Industries, Ltd., Osaka, Japan (non-U.S. corporation)
PI US 6166221 20001226
AI US 2000-511782 20000223 (9)
RLI Division of Ser. No. US 355096
PRAI JP 1997-10114 19970123
DT Utility
FS Granted
EXNAM Primary Examiner: McKane, Joseph K.; Assistant Examiner: Wright, Sonya
LREP Winderoth, Lind & Ponack, L.L.P.
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 673
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a method for producing an optically active 4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoic acid or a pharmaceutically acceptable salt thereof, which includes subjecting a compound of the formula (I) wherein each symbol in the formula is as defined in the specification, to optical resolution by fractional crystallization to give an optically active compound thereof and subjecting the compound to hydrolysis reaction. According to this method, a resolution method useful for industrial large-scale production of the optically active compound of 4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoic acid, which is useful as a thromboxane synthetase inhibitor and an agent for the prophylaxis and treatment of diabetic complications, can be obtained.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 52 OF 58 USPATFULL
AN 2000:64963 USPATFULL
TI Process for producing optically active imidazole compounds, intermediates for synthesizing the same, and process for producing the same
IN Kawasaki, Kazuyuki, Fukuoka, Japan
Kobayashi, Haruhito, Fukuoka, Japan
Ehara, Syuji, Fukuoka, Japan
Sato, Hideaki, Fukuoka, Japan
PA Yoshitomi Pharmaceutical Industries, Ltd., Japan (non-U.S. corporation)
PI US 6066739 20000523
WO 9832740 19980730
AI US 1999-355096 19990723 (9)
WO 1998-JP150 19980114

19990723 PCT 371 date
19990723 PCT 102(e) date
PRAI JP 1997-10114 19970123
DT Utility
FS Granted
EXNAM Primary Examiner: McKane, Joseph
LREP Wenderoth, Lind & Ponack, L.L.P.
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 622
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a method for producing an optically active 4-[.alpha.-hydro-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoic acid or a pharmaceutically acceptable salt thereof, which includes subjecting a compound of the formula (I) ##STR1## wherein each symbol in the formula is as defined in the specification, to optical resolution by fractional crystallization to give an optically active compound thereof and subjecting the compound to hydrolysis reaction. According to this method, a resolution method useful for industrial large-scale production of the optically active compound of 4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoic acid, which is useful as a thromboxane synthetase inhibitor and an agent for the prophylaxis and treatment of diabetic complications, can be obtained.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 53 OF 58 USPATFULL
AN 2000:57790 USPATFULL
TI Prophylaxis and treatment of diabetic complications with 4-[.alpha.-hydroxy-2-methyl-5-(1-imidazolyl) benzyl]-3,5-dimethylbenzoic acid
IN Hayashi, Yoshiharu, Iruma, Japan
Goto, Nobuharu, Iruma, Japan
PA Yoshitomi Pharmaceutical Industires, Ltd., Japan (non-U.S. corporation)
PI US 6060496 20000509
WO 9724333 19970710
AI US 1998-91993 19980626 (9)
WO 1996-JP3776 19961224
19980626 PCT 371 date
19980626 PCT 102(e) date
PRAI JP 1995-340161 19951227
DT Utility
FS Granted
EXNAM Primary Examiner: Higel, Floyd D.
LREP Wenderoth, Lind & Ponack, L.L.P.
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 603
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to an agent for the prophylaxis and treatment of diabetic complications comprising, as an active ingredient, 4-[.alpha.-hydroxy-2-methyl-5-(1-imidazolyl) benzyl]-3,5-dimethylbenzoic acid, an optically active compound thereof or a pharmaceutically acceptable salt thereof. The present invention further relates to a method for the prophylaxis and treatment of diabetic complications comprising administering an effective amount of this compound. The medicament of the present invention is useful for the prophylaxis and

treatment of diabetic complications, namely, diabetic neuropathy, nephropathy, ophthalmopathy, arteriosclerosis and the like. The action of the drug is long-lasting for very small doses and a single administration a day is sufficient.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 54 OF 58 USPATFULL
AN 92:14818 USPATFULL
TI Pharmaceutical composition with improved dissolution property
IN Oda, Minoru, Nakatsu, Japan
Kino, Shigemi, Chikujo, Japan
Ogawa, Kenji, Chikujo, Japan
Shiotsuki, Takako, Chikujo, Japan
PA Yoshitomi Pharmaceutical Industries, Ltd., Osaka, Japan (non-U.S. corporation)
PI US 5091191 19920225
WO 8906959 19890810
AI US 1989-415356 19890925 (7)
WO 1989-JP100 19890131
19890925 PCT 371 date
19890925 PCT 102(e) date
PRAI JP 1988-23250 19880203
DT Utility
FS Granted
EXNAM Primary Examiner: Page, Thurman K.; Assistant Examiner: Webman, E. J.
LREP Wenderoth, Lind & Ponack
CLMN Number of Claims: 2
ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 297
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A pharmaceutical composition of the active agent sodium 4-[.alpha.-hydroxy-5-(1-imidazolyl)-2-methylbenzyl]-3,5-dimethylbenzoate (a thromboxane synthetase inhibitor for treatment of diseases such as thrombosis and asthma) or its optical isomer or its hydrate with an improved dissolution property, which comprises D-mannitol and/or sodium hydrogencarbonate and at least one water-soluble polymer.

The pharmaceutical composition is such that the dissolution of the above-mentioned active agent is free from pH dependency in the digestive tract including the stomach.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 55 OF 58 USPATFULL
AN 90:38442 USPATFULL
TI Therapeutic agents
IN Smithers, Michael J., Macclesfield, United Kingdom
PA Imperial Chemical Industries PLC, London, United Kingdom (non-U.S. corporation)
PI US 4925869 19900515
AI US 1987-118227 19871103 (7)
PRAI GB 1986-26296 19861104
DT Utility
FS Granted
EXNAM Primary Examiner: Burgess Yarbrough, Amelia
LREP Cushman, Darby & Cushman
CLMN Number of Claims: 14
ECL Exemplary Claim: 1

09/979,509

DRWN No Drawings
LN.CNT 1260
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns novel therapeutic agents containing a (Z)-(2-alkoxyalkyl- or 2-aryloxyalkyl-4-phenyl-1,3-dioxan-5-yl)alkenoic acid, or a related tetrazole derivative, which antagonizes one or more of the actions of thromboxane A.sub.2, together with a compound which inhibits the synthesis of thromboxane A.sub.2. The compositions are useful as medicines in treating a variety of diseases or medical conditions in which thromboxane A.sub.2 and/or other prostanoid contractile substances are involved.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 56 OF 58 USPATFULL
AN 90:19583 USPATFULL
TI Pharmaceutical compositions
IN Brewster, Andrew G., Macclesfield, United Kingdom
Brown, George R., Wilmslow, United Kingdom
Smithers, Michael J., Macclesfield, United Kingdom
PA Imperial Chemical Industries plc, London, England (non-U.S. corporation)
PI US 4908380 19900313
AI US 1987-118226 19871103 (7)
PRAI GB 1986-26297 19861104
DT Utility
FS Granted
EXNAM Primary Examiner: Yarbrough, Amelia Burgess
LREP Cushman, Darby & Cushman
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1314
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention concerns novel pharmaceutical compositions containing a 4(Z)-6-(2,4-diphenyl-1,3-dioxan-5-yl)-alkenoic acid which antagonizes one or more of the actions of thromboxane A.sub.2, together with a compound which inhibits the synthesis of thromboxane A.sub.2. The compositios are useful as medicines in treating a variety of diseases or medical conditions in which thromboxane A.sub.2 and/or other prostanoid contractile substances are involved.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 57 OF 58 USPATFULL
AN 87:30374 USPATFULL
TI Imidazole derivatives
IN Tsuruda, Mineo, Fukuoka, Japan
Oe, Takanori, Nakatsu, Japan
Kawasaki, Kazuyuki, Buzen, Japan
Mikashima, Hiroshi, Fukuoka, Japan
Yasuda, Hiroshi, Nakatsu, Japan
PA Yoshitomi Pharmaceutical Industries, Ltd., Osaka, Japan (non-U.S. corporation)
PI US 4661603 19870428
AI US 1986-823633 19860129 (6)
RLI Continuation-in-part of Ser. No. US 1983-556231, filed on 31 Oct 1983, now patented, Pat. No. US 4581369, issued on 8 Apr 1986
PRAI JP 1982-34365 19820303
JP 1985-121220 19850603
DT Utility

09/979,509

FS Granted
EXNAM Primary Examiner: Brust, Joseph Paul
LREP Wenderoth, Lind & Ponack
CLMN Number of Claims: 3
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 739
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB .alpha.-(2,6-dimethyl-4-carboxyphenyl)-2-methyl-5-(1-imidazolyl)-benzenemethanol, pharmaceutically acceptable metal salts forms thereof, acid addition salt forms thereof, amino acid addition salt forms thereof, hydrate forms thereof and mixtures thereof.

Such compounds have inhibitory activities on biosynthesis of thromboxane A.sub.2, inhibitory activities on platelet aggregation, vasodilative activities and protective effects against liver disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L4 ANSWER 58 OF 58 USPATFULL
AN 86:20284 USPATFULL
TI Imidazole derivatives
IN Tsuruda, Mineo, Fukuoka, Japan
Oe, Takanori, Nakatsu, Japan
Kawasaki, Kazuyuki, Buzen, Japan
Mikashima, Hiroshi, Fukuoka, Japan
Yasuda, Hiroshi, Nakatsu, Japan
PA Yoshitomi Pharmaceutical Industries, Ltd., Osaka, Japan (non-U.S. corporation)
PI US 4581369 19860408
WO 8303096 19830915
AI US 1983-556231 19831031 (6)
WO 1983-JP60 19830228
19831031 PCT 371 date
19831031 PCT 102(e) date
PRAI JP 1982-34365 19820303
DT Utility
FS Granted
EXNAM Primary Examiner: Brust, Joseph Paul
LREP Wenderoth, Lind & Ponack
CLMN Number of Claims: 11
ECL Exemplary Claim: 1,11
DRWN No Drawings
LN.CNT 628
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB An imidazole derivative of the formula: ##STR1## wherein each of R.sup.1 and R.sup.4 is a hydrogen atom or a lower alkyl group; each of R.sup.2 and R.sup.3 is a hydrogen atom, a halogen atom, a hydroxyl group, a lower alkyl group, a lower alkoxy group, an aralkyloxy group, a nitro group or an amino group; A is --O--, --S--, --CH.dbd.CH-- pr --CH.dbd.N--; Z is an aryl group, a thienyl group, a pyridyl group or a furyl group, in which definition these aromatic (heterocyclic) rings may have 1 to 3 substituents, each substituent being independently selected from a halogen atom, a lower alkyl group, a cyclic alkyl group, a lower alkoxy group, a hydroxyl group, a carboxyl group, a lower alkoxycarbonyl group, a carboxy-lower-alkoxy group, a di-lower-alkylamino-lower-alkoxy group and a nitro group; and a pharmaceutically acceptable acid addition salt thereof, a method for preparing the same and a pharmaceutical composition containing such compound. Such compounds have inhibitory activities on biosynthesis of thromboxane A.sub.2, inhibitory activities

on platelet aggregation, vasodilative activities and protective effects on liver disorders.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

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